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10/551,304	05/18/2006	Christopher R Trotta	10589-033-999	6447

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EXAMINER	
LIU, SUE XU	
ART UNIT	PAPER NUMBER
1639	
MAIL DATE	DELIVERY MODE
03/17/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/551,304	TROTTA, CHRISTOPHER R	
	Examiner	Art Unit	
	SUE LIU	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42-82* is/are pending in the application.

4a) Of the above claim(s) *44,47,49-61 and 65-82* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42,43,45,46,48 and 62-64* is/are rejected.

7)☒ Claim(s) *48 and 63* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/20/07; 12/27/07* .
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

1. Claims 1-41 have been canceled.

Claims 42-82 are currently pending.

Claims 44, 47, 49-61, 65, 66 and 67-82 have been withdrawn.

Claims 42, 43, 45, 46, 48 and 62-64 are being examined in this application.

Election/Restrictions

2. Applicant's election of Group 1 (claims 42-66) in the reply filed on 12/22/08 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. Applicant's election without traverse of the following species:

A.) reduces fungal tRNA splicing endonuclease activity;

B.) intact cells;

C.) a reporter gene assay;

in the reply filed on 12/22/08 is acknowledged. Applicants also state "claims 42, 43, 45, 46, 48, 62, 63 and 64 read on the elected species." Accordingly, Claims 44, 47, 49-61, 65 and 66 are withdrawn due to non-elected species.

Priority

4. This application is filed under 35 U.S.C 371 of PCT/US04/09574 (filed on 03/26/2004), which claims priority to US provisional applications 60/458,090 (filed on 3/27/2003).

Information Disclosure Statement

5. The IDS filed on 7/20/07 and 12/27/07 have been considered. See the attached PTO 1449 forms. Please note the crossed out references due to lack of dates or English Translations.

Specification

6. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification. MPEP 608.01.

Claim Objections

7. Claim 48 is objected to because the said claim depends on a non-elected claim (Claim 47) that is drawn to a non-elected invention.

Claim 63 is objected to because the said claim depends on a non-elected claim (Claims 53 and 59) that is drawn to a non-elected invention.

Appropriate correction is requested.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description Rejection

9. Claims 42, 43, 45, 46, 48 and 62-64 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims recite "A method for identifying a compound that modulates fungal tRNA splicing endonuclease activity, the method comprising:

(a) contacting a compound or a member of a library of compounds with a fungal tRNA splicing endonuclease and a substrate for tRNA splicing endonuclease comprising a nucleic acid, wherein the nucleic acid comprises a tRNA intron within a bulge-helix-bulge structure or a mature domain of a precursor tRNA; and

(b) detecting the amount of substrate cleaved, wherein a compound that modulates fungal tRNA splicing endonuclease activity is identified if the amount of substrate cleaved in the presence of a compound is altered relative to the amount of substrate cleaved in the absence of the compound or in the presence of a negative control."

To satisfy the written description requirement, applicants may convey reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention.

Applicants may show possession of an invention by disclosure of drawings or structural chemical formulas that are sufficiently detailed to show that applicant was in possession of the claimed invention as a whole. See, e.g., Vas-Cath, 935 F.2d at 1565, 19 USPQ2d at 1118.

The written description requirement of 35 U.SC. 112 exists independently of enablement requirement, and the requirement applies whether or not the case involves questions of priority. The requirement applies to all inventions and includes chemical inventions. The fact that the patent is directed to method entailing use of compounds, rather than to compounds per se, does not remove patentee's obligation to provide a description of the compound sufficient to

distinguish infringing methods from non-infringing methods. See Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 920-23, 69 USPQ 2d 1886, 1890-93 (Fed. Cir. 2004).

With regard to the description requirement, applicants' attention is invited to consider the decision of the Court of Appeals for the Federal Circuit, which holds that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it form other materials." University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1405 (1997), quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original) [The claims at issue in University of California v. Eli Lilly defined the invention by function of the claimed DNA (encoding insulin)].

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species or by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See Eli Lilly, 119 F. 3d at 1568, 43 USPQ2d at 1406.

The instant Claim 42 is drawn to a genus of method of using various reagents and/or steps. Claim 42 is drawn to a genus of "fungal tRNA splicing endonucleases" and a genus of "substrate" for the endonucleases. Neither the instant specification nor the claims have demonstrated common structure and/or function for the claimed genus of endonucleases and the genus of corresponding substrates. In addition, no representative numbers of species for each claimed genus is provided to show possession of the claimed genuses.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. (see MPEP 2163 II).

In this case, the instant application only provides one example of a yeast tRNA splicing endonuclease and its corresponding substrate. It is not clear if the yeast endonuclease is

representative of the claimed entire genus of "fungal tRNA splicing endonucleases", and if the yeast tRNA substrate is representative of the entire genus of fungal substrates.

The state of art at the time of filing also does not provide for all "fungal tRNA splicing endonucleases" and their corresponding substrates. It is not predictably known what specific polypeptide sequences and/or structures are required for a fungal tRNA splicing endonuclease, and what specific nucleic acid sequences and/or structures are required for its corresponding substrate. As the instant claimed methods require the components of the endonuclease and its substrate, the possession of the said components have to be demonstrated to show possession of the instant claimed methods.

Therefore, applicant does not appear to have possession of the claimed genus of enzymes and its substrate. Applicant's claimed scope represents only an invitation to experiment regarding possible fungal tRNA splicing endonuclease and its substrates that might be identified and used for the purpose of screening for a splicing inhibitor.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

(Note: the instant claim numbers are in bold font.)

Tocchini-Valentini and Gontarek

11. Claims 42, 43, 45, 46, 48 and 62-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Tocchini-Valentini** et al (WO 01/92463; 12/6/2001; Cited in IDS), in view of **Gontarek** (WO 00/67580; 11/16/2000; cited in IDS).

The instant claims recite "A method for identifying a compound that modulates fungal tRNA splicing endonuclease activity, the method comprising:

(a) contacting a compound or a member of a library of compounds with a fungal tRNA splicing endonuclease and a substrate for tRNA splicing endonuclease comprising a nucleic acid, wherein the nucleic acid comprises a tRNA intron within a bulge-helix-bulge structure or a mature domain of a precursor tRNA; and

(b) detecting the amount of substrate cleaved, wherein a compound that modulates fungal tRNA splicing endonuclease activity is identified if the amount of substrate cleaved in the presence of a compound is altered relative to the amount of substrate cleaved in the absence of the compound or in the presence of a negative control."

Tocchini-Valentini et al., throughout the publication, teaches methods of monitoring tRNA splicing endoclease activity on various target molecules (e.g. Abstract). The reference teaches contacting a substrate for tRNA splicing endonuclease with a tRNA splicing endonuclease (e.g. pp.6+; Figures), which read on the tRNA splicing endonuclease and the substrate of step (a) **clm 42**. The reference also teaches the substrate contain "bulge-helix-bulge" structure (e.g. pp.6+; Figure 5). The reference also teaches detecting the amount of substrate cleaved (e.g. p.7+; Figures; Claims), which reads on the detecting substrate cleaved of step (b) of

clm 42. The reference also teaches the tRNA splicing endonuclease is from yeast (e.g. p.16, [0054]; p.8), which reads on the "fungal tRNA splicing endonuclease" of **clm 42**.

The reference also teaches the substrate with the bulge-helix-bulge structure is part of a reporter gene (e.g. GFP) (e.g. Figure 5; p.4; p.25), which reads on the reporter gene of **clms 45** and **62**.

The reference also teaches detecting the GFP expression as an indication of the endonuclease activity (e.g. p.25; Figures), which reads on the reporter activity step of **clms 46** and **48**.

The reference also teaches endonuclease from yeast such as S. cerevisiae (e.g. p.16). The reference also teaches using endogenous tRNA splicing endonuclease in in vivo experiments (e.g. p.8).

Tocchini-Valentini et al do not explicitly teach assaying for a compound that can reduce (or inhibitor) RNA splicing as recited in **clms 42**, **43**, **46** and **48**. The reference also does not explicitly teach using a fungal cell such as a yeast cell as recited in **clm 46**, **63** and **64**.

However, **Gontarek**, throughout the publication, teaches methods or assays for screening for compound that modulate splicing reactions. (e.g. Abstract). The reference teaches contacting a compound to a splicing reaction to "inhibit" the splicing reaction (e.g. Claim 1; p.2). The reference also teaches screening for compounds that modulate splicing reactions using in vivo splicing reactions (i.e. in intact cells) (e.g. Abstract). The reference also teaches the method of screening compounds can be used to identify inhibitors of "splicing polypeptides" so that "fungistatic and/or fungicidal" compounds can be identified. (e.g. p.23, lines 3+). The reference also teaches using yeast cells (such as S. cerevisiae) as host cells (e.g. p.18, lines 28+).

Therefore, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to screening for inhibitors of RNA splicing such as tRNA splicing by contacting cells (comprising splicing reaction components) such as yeast cells with a compound of interest.

A person of ordinary skill in the art would have been motivated at the time of the invention was made to contact cells with compounds of interest to measure the amount of RNA splicing, because Gontarek teaches the need to screen for compounds that are inhibitor of RNA splicing mechanism so that various useful compounds such as fungicidal compounds can be identified. It would have been obvious to a person of ordinary skill in the art to try various combinations of the known methods of screening for compounds of interested based their abilities to inhibit RNA splicing in cells, methods of detecting RNA splicing using tRNA splicing endonuclease with the appropriate substrate, etc., in an attempt to optimize and/or improve the screening method of detecting RNA splicing inhibitors in cells, as a person with ordinary skill has good reason to pursue the known options within his or her technical grasp.

A person of ordinary skill in the art would have been motivated at the time of the invention was made to use yeast cells as for the screening assay, because Tocchini-Valentini et al and Gontarek teach the need to use yeast cells as the cells would offer endogenous tRNA splicing endonuclease. In addition, because both the cited references teach methods of using yeast cells and/or other cells for in vivo splicing experiments to assay for RNA splicing, it would have been obvious to one skilled in the art to substitute one type of cells for the other to achieve the predictable result of assaying for RNA splicing in the presence or absence of a compound of interest.

A person of ordinary skill in the art would have reasonable expectation of success of achieving such modifications since the cited references have demonstrated the success of detecting the amount of tRNA splicing endonuclease activity using appropriate substrate using a reporter gene system in an in vivo system and the success of using an in vivo system to screen for an inhibitor of RNA splicing mechanism.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached at 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Sue Liu/
Patent Examiner, AU 1639
3/6/09